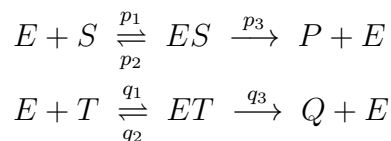


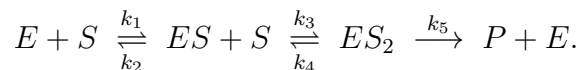
*Read:* Chapter 2.3: Modeling biochemical reactions with differential equations, by R. Robeva, and N. Yildirim. pages 40–46.

1. Consider the reactions where two substrates  $S$  and  $T$  compete for binding to an enzyme  $E$  to produce two different products  $P$  and  $Q$ :



Assume that each reaction follows the Michaelis-Menten kinetics. Also, assume that the initial enzyme concentration is  $E_0 = [E] + [ES] + [ET]$ .

- (a) Derive rate equations for  $P$  and  $Q$  in this system in terms of  $[ES]$  and  $[ET]$ . That is, determine  $d[P]/dt$  and  $d[Q]/dt$ .
  - (b) Derive rate equations for  $ES$  and  $ET$ .
  - (c) Assume that the enzyme-substrate complexes reach equilibrium quickly:  $d[ES]/dt \approx 0$  and  $d[ET]/dt \approx 0$ . Solve for  $[E]$  in each of these equations.
  - (d) Equate the two expressions for  $[E]$  from Part (c) and solve for  $[ET]$ .
  - (e) Solve for  $[ES]$  by plugging your answers to Parts (c) and (d) into  $E_0 = [E] + [ES] + [ET]$ . You should not have  $[E]$  or  $[ET]$  in your final answer.
  - (f) Plug this into the original ODE for  $d[P]/dt$ .
  - (g) Repeat the previous three steps but solve for  $[ES]$  instead of  $[ET]$ .
  - (h) Explain the effects of the competition occurring.
2. The Hill equation is an approximation for multi-molecule binding and it assumes simultaneous binding of  $n$ -molecules of a substrate  $S$  to the enzyme  $E$ . Suppose that two molecules of the substrate  $S$  are undergoing a reaction with an enzyme in an ordered manner as follows:



Assume that the reaction follows the Michaelis-Menten kinetics and that the initial enzyme concentration is  $E_0 = [E] + [ES] + [ES_2]$ .

- (a) Derive rate equations for  $P$ ,  $ES$ , and  $ES_2$ . Be *very* careful with the  $ES \xrightarrow{k_2} E + S$  reaction when deriving the equation for  $[ES]$ .
- (b) Assume that  $d[ES_2]/dt \approx 0$  and solve for  $[ES]$ .
- (c) Assume that  $d[ES]/dt \approx 0$ . Plug your answer to Part (b) into this and solve for  $[E]$ .
- (d) Plug your expressions for  $[E]$  and  $[ES]$  back into  $E_0 = [E] + [ES] + [ES_2]$  and solve for  $[ES_2]$ .
- (e) Derive an ODE for  $[P]$  of the form  $d[P]/dt = f([S])$ .

(f) Compare your answer to Part (d) to the Hill equation with Hill coefficient  $n = 2$ :

$$\frac{d[P]}{dt} = \frac{V_{\max}[S]^2}{K_m + [S]^2}.$$

When do these two equations become roughly the same?